

U.S. SERIAL NO: 08/126,505
FILED: September 24, 1993
AMENDMENT

C2
Ent
sequence for DAF. Sequence ID No. 18 is the nucleotide sequence
and Sequence ID No. 19 is the amino acid sequence for MCP.--

In the Claims

C3
sub
D'
1. (twice amended) An analog of a protein regulating
complement activation having short consensus repeats of amino
acid sequence selected from the group complement regulating
proteins consisting of complement receptor 1, complement receptor
2, decay accelerating factor, membrane cofactor protein, C4
binding protein, and factor H, and those complement regulating
proteins wherein the carboxy terminus is removed to allow the
protein to be secreted, wherein said protein analog is selected
from the group consisting of complement regulating [proteins]
protein analogs containing short consensus repeats derived from a
second, different complement regulating protein, complement
regulating [proteins] protein analogs wherein the short consensus
repeats are rearranged[, complement regulating proteins having
defined amino acid substitutions in the short consensus repeats
selected from the group consisting of repeats having binding
activity, cofactor activity, and decay accelerating activity,
wherein the substitution alters the activity of the naturally
occurring complement regulatory protein], and complement
regulating [proteins] protein analogs consisting of as few as
three short [consenses] consensus repeats, wherein the protein
analog binds C3b, C4b or C3b and C4b.

C3
Cont

2. (amended) The analog of claim 1 wherein the complement regulatory protein analog has an activity [is] selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, C4b cofactor activity, and decay accelerating activity.

Please cancel claims 6 and 7.

8. (amended) The analog of claim 2 wherein the protein contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:

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CR1-4 with its first 122 amino acids (SCR1-2) replaced with CR1 amino acids 497-618 (SCR 8-9) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with: T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-P-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K, or structurally similar amino acids.

9. (amended) The analog of claim 2 wherein the protein contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:

79: D; 37,39: Y,D; 92: T; 109-112: N-A-A-H; 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q; 114-117, 121: N-A-A-H, S-T-K-P...Q; 116: K; 116,117: K-P; 92-94: K...Y; 99,103,106: S...T...I; 109-112: P-T-V-I; 110: T; 111: V; 112: I; 114: D; 115: N; 121: D; 117: T; 1,3: Q...N; 6-9: E-W-L-P; 12-16, 18-21: K-L-K-T-Q...N-A-

S-D; 27,29: S...K; 37: S; 44, 47, 49: I...K...S; 52-54, 57, 59:
T-G-A...R...R; 78-79, 82: K-G...F; 85, 87: Q...K; 12-16, 18-21:
R-P-T-N-L...D-E-R-E; 27,29: Y...N; 35, 64-65, 94: G...R-N...Y,
substitutions with structurally similar amino acids, and
combinations thereof.

C4
Cont

10. (amended) The analog of claim 2 wherein the
complement regulatory protein is decay accelerating factor
wherein one or more substitutions are introduced into the region
of the protein corresponding to decay accelerating factor short
consensus repeats SCRs 2-3 as shown in Sequence ID No. 17
selected from the group consisting of 180-187: S-T-K-P-P-I-C-
Q; 175-178: N-A-A-H; 175-187: S-T-K-P-P-I-C-Q-N-A-A-H; 130: R;
145: D; 77-84: K-L-K-T-Q-T-N-A-S-D; 90-92: S-L-K, substitutions
with structurally similar amino acids, and combinations thereof.

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14. (amended) The analog of claim 1 wherein the
region of the protein having biological activity consists
[essentially] of three short consensus regions and has two
complement regulatory activities.

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E3

16. (twice amended) A method for making an analog of
a protein regulating complement activation having short consensus
repeats of amino acid sequence selected from the group consisting
of complement receptor 1, complement receptor 2, decay
accelerating factor, membrane cofactor protein, C4 binding
protein, and factor H, and these complement regulating proteins

wherein the carboxy terminus is removed to allow the protein to be secreted, comprising

constructing a DNA sequence encoding a protein analog selected from the group consisting of complement regulating [proteins] protein analogs containing short consensus repeats derived from a second, different complement regulating protein, complement regulating [proteins] protein analogs wherein the short consensus repeats are rearranged[, complement regulating proteins having defined amino acid substitutions in the short consensus repeats selected from the group consisting of repeats having binding activity, cofactor activity, and decay accelerating activity, wherein the substitution alters the activity of the naturally occurring complement regulatory protein], and complement regulating [proteins] protein analogs consisting of as few as three short [consenses] consensus repeats, wherein the protein analog binds C3b, C4b, or C3b and C4b, and

expressing the DNA sequence in a suitable host for expression of the protein.

17. (amended) The method of claim 16 wherein the complement regulatory protein analog has an activity [is] selected from the group consisting of C3b binding activity, C3b cofactor activity, C4b binding activity, C4b cofactor activity, and decay accelerating activity.

Please cancel claims 21 and 22.

23. (amended) The method of claim 17 wherein the protein analog contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:

CR1-4 with its first 122 amino acids (SCR1-2) replaced with CR1 amino acids 497-618 (SCR 8-9) and CR1-4(8,9) with deletion of 194-253; substitution of amino acids 271-543 with:
T-R-T-T-F-H-L-G-R-K-C-S-T-A-V-S-D-A-T-T-S-E-G-L-R-L-C-A-A-H-P-R-E-T-G-A-L-Q-P-P-H-V-K, or structurally similar amino acids.

24. (amended) The method of claim 17 wherein the protein analog contains a change within a short consensus repeat that corresponds with a change to complement receptor one as shown in Sequence ID No. 13 selected from the group consisting of:

79: D; 37,39: Y,D; 92: T; 109-112: N-A-A-H; 109-112, 114-117, 121: N-A-A-H, S-T-K-P...Q; 114-117, 121: N-A-A-H, S-T-K-P...Q; 116: K; 116,117: K-P; 92-94: K...Y; 99,103,106: S...T...I; 109-112: P-T-V-I; 110: T; 111: V; 112: I; 114: D; 115: N; 121: D; 117: T; 1,3: Q...N; 6-9: E-W-L-P; 12-16, 18-21: K-L-K-T-Q...N-A-S-D; 27,29: S...K; 37: S; 44, 47, 49: I...K...S; 52-54, 57, 59: T-G-A...R...R; 78-79, 82: K-G...F; 85, 87: Q...K; 12-16, 18-21: R-P-T-N-L...D-E-R-E; 27,29: Y...N; 35, 64-65, 94: G...R-N...Y,

substitutions with structurally similar amino acids, and combinations thereof.

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Cont

25. (amended) The method of claim 17 wherein the complement regulatory protein is decay accelerating factor wherein one or more substitutions are introduced into the region of the protein corresponding to decay accelerating factor short consensus repeats SCRs 2-3 as shown in Sequence ID No. 17 selected from the group consisting of 180-187: S-T-K-P-P-I-C-Q; 175-178: N-A-A-H; 175-187: S-T-K-P-P-I-C-Q-N-A-A-H; 130: R; 145: D; 77-84: K-L-K-T-Q-T-N-A-S-D; 90-92: S-L-K, substitutions with structurally similar amino acids, and combinations thereof.

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27. (amended) The method of claim 16 comprising inserting into the protein analog at least one short consensus repeat derived from a different protein selected from the group consisting of complement receptor 1, complement receptor 2, decay accelerating factor, membrane cofactor protein, C4 binding protein, and factor H.

C9
Def 7D

34. (twice amended) A method for enhancing the C4b or C3b cofactor activity of a complement regulatory protein, wherein the protein has either C3b or C4b cofactor activity, comprising adding sequences to the protein conferring binding of the other ligand, either C4b or C3b, wherein the sequences are present in a protein selected from the group of naturally occurring complement